

detecting a change of the incident light or a change of a reflected light thereof when said resonance phenomenon is generated; and

recognizing an amount of said medical substance (antigen) contained in said sample on the basis of said change of the incident light or the reflected light.

### **REMARKS**

This is in response to the Office Action of August 17, 1999 in which the Examiner:

(a) objected to the drawings because the antigen fixed to another surface of the metal film as recited in claims 20 and 23 is not shown;

(b) found claims 14-27 to be indefinite because, inter alia, it was not clear to the Examiner whether the antigen fixed to resonance material is the "medical substance" or a reagent for detection of the "medical substance";

(c) found claims 14, 15, 17, 19, 22, 24, 25 and 27 to be anticipated by Batchelder (U.S. Patent No. 4,844,613);

(d) found claims 14, 15, 17, 19, 22, 24, 25 and 27 to be anticipated by Finlan (U.S. Patent 4,997,278);

(e) found claims 14, 15, 17, 19, 22, 24,, 25 and 27 to be anticipated by Finlan (U.S. Patent No. 5,047,213); and

(f) found claims 14, 16, 22 and 24 to be anticipated by Stewart (U.S. Patent 5,229,833).

Based on the above amendments and following remarks, the application is deemed to be in condition for allowance and action to that end is respectfully requested.

## **I. APPROPRIATENESS OF AMENDMENT**

The amendment herein is appropriate as they do not raise new issues. The amendments are quite minor and merely clarify the invention. The sole substantive amendment of "a medical substance" into "a medical substance (an antigen)" is only to make clear that the antigen fixed to the resonance material is the "medical substance" and that an antibody is coupled with the antigen in a specific manner, because the Examiner is confused with those features.

## **II. THE INVENTION**

The present invention relates to a medical substance measuring apparatus in which a medical substance is measured by using a resonance phenomenon resonating with an evanescent wave and related to a medical substance sensor for use in the apparatus. A major feature of the present invention is that the medical substance to be measured by the apparatus is fixed to a resonance material as an antigen.

## **III. THE SECTION 112 REJECTION SHOULD BE WITHDRAWN**

The Examiner appears to assert that the current claims do not clearly define the presence of an antigen on the resonance material, wherein the antigen is the analyte that is to be detected. Submitted are amended claims which clarify the unclear points **without broadening the scope of the claims and without raising "new issues."**

For example, claim 14 has been amended to clarify that the antigen fixed to the resonance material is "a medical substance," not a reagent for detection of the medical substance.

In claims 20 and 23, the Examiner pointed out that it is not clear as to how the antigen can be fixed to a surface of the metal film which is opposite to the surface prism when the metal

film is formed on the surface of the prism. The unclear portion of this claim has been deleted.

Claim 24 has been amended to address the points raised by the Examiner, for instance, as to whether the antibody is coupled to the medical substance and is specific for the antigen or the medical substance, and as to the mixture which is deemed to be redundant because the antibody is already in contact with the resonance material.

As explained, none of the amendments raise new issues (see Section I). The Section 112 rejection should therefore be withdrawn.

**IV. THE OBJECTION TO THE DRAWINGS HOULD BE WITHDRAWN**

As the unclear portions regarding the antigen fixed to a metal film in Claims 20 and 23 have been deleted as stated above, the objection to the drawings should be withdrawn.

**V. THE NEWLY REVISED CLAIMS ARE CLEARLY PATENTABLE OVER THE PRIOR ART**

As mentioned in the specification on page 4, line 28 to page 5, line 24, according to previously known methods, it has been tried to measure in a medical substance that an antibody is fixed to a resonance material, such as a metal thin film, and the medical substance (antigen) which is coupled to the antibody in a specific manner is detected directly. However, the medical substance contained in a body liquid, such as urine or blood, has a significantly small molecular weight; therefore, even if the medical substance is reacted with the antibody fixed to the resonance material (antigen-antibody reaction), the change of the resonance angle, etc. is extremely small. Therefore, it is very difficult to detect such a medical substance by conventional methods.

The present invention provides an apparatus for detecting a medical substance using a resonance phenomenon resonating with an evanescent wave, by which even a medical substance having a small molecular weight can be detected. Thus, a medical substance to be measured by the apparatus is previously fixed to the resonance material as an antigen; a known amount of an antibody is mixed in a sample; the antibody is brought in contact to the resonance material on which the antigen (medical substance to be detected) has been fixed; then the change of the condition for generating the resonance phenomenon (resonance angle, etc.) is observed when an antigen-antibody reaction is caused. Since an antibody has a significantly greater molecular weight, when such an antibody is coupled with the antigen (medical substance to be detected) fixed on the resonance material, the change of the condition, i.e. resonance angle, etc. is sufficiently great to be detected. It should be noted that the amount of the antibody mixed in the sample is previously known, so that the amount of the medical substance contained in the sample can be indirectly calculated from the change of the condition.

The Examiner asserts that "If the 'medical substance' is an antigen, then a specific binding reagent such as an antibody specific for the antigen would be required on the resonance material to provide for detection of the antigen." First, the confusion herein is resolved by the amendments presented. Second, it is respectfully submitted that the Examiner's assertion is proper for the conventional detecting technology. However, as described above, the present invention has a feature that not an antibody but the medical substance to be detected, per se, which is an antigen, is fixed on the resonance material. This is greatly different from the conventional technology, because such construction makes it easy to detect the medical substance having a very small molecular weight! The references cited by the Examiner disclose

a sensor for detecting a specific substance by using a surface plasmon resonance phenomenon. However, the substance fixed to the resonance material is not an antibody but an antigen. None of the references disclose, teach or otherwise suggest a measuring apparatus of a sensor where a medical substance (antigen) to be measured is fixed to a resonance material as recited in new independent claims 14 and 24. Further, according to the present invention, such a medical substance having an extremely small molecular weight, which has a difficulty to be detected by the conventional technique, can be easily detected and is thus clearly non-obvious over the prior art. In view of the above, Independent Claims 14 and 24, which recite the distinctive features, are allowable.

Each remaining claim is dependent, directly or indirectly, on Claims 14 and 24, and are also allowable for the same reasons.

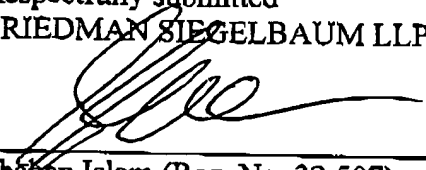
### CONCLUSION

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance and allowance of the application is respectfully requested.

Should the Examiner require or consider it advisable that the specification, claim and/or drawings be further amended or corrected in formal respects in order to place the case in condition for final allowance, then it is respectfully requested that such amendment or correction be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the

Examiner feel that the personal discussion might be helpful in advancing this case to allowance,  
the Examiner is invited to telephone the undersigned.

Respectfully submitted  
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